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10/516,619	05/25/2005	Andreas Bergmann	2582.021	7129

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EXAMINER	
WEN, SHARON X	
ART UNIT	**PAPER NUMBER**
1644	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,619	BERGMANN, ANDREAS	
	Examiner	Art Unit	
	Sharon Wen	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-13* is/are pending in the application.

4a) Of the above claim(s) *11-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 12/26/2006, has been entered.

Claims 1-8 have been canceled.

Claims 9-13 have been added and are currently pending

2. Text of those sections of Title 35 U.S.C. not included in this Action can be found in a prior Action.

This Action will be in response to Applicant's Arguments/Remarks, filed 07/26/2007.

The rejections of record can be found in the previous Office Action.

Election/Restrictions

3. Applicant's election of the species that reads on "*administration of an agent which binds or blocks anti-AG_{m1} antibodies and/or anti-Gm1 antibodies*" and the ganglioside AG_{m1} as the species of "agent" that in the reply filed on 09/10/2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 11-13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Invention and/or Species, there being no allowable generic or linking claim.

Claims 9-10 are currently under examination as they read on a method for prevention inhibition and treatment of sepsis in an animal or patient comprising administering an agent wherein the agent read on the elected species, AG_{m1}.

Specification

4. Applicant's amendment to the specifications, filed 12/03/2004, has been acknowledged.

Priority

5. The priority date for claims 9-10 is deemed the effective filing date of PCT/EP03/03448, i.e., 04/02/2003.

Applicant's foreign priority claim is acknowledged. However there deos not appear to be a certified translation of the foreign priority application, 02012515.9. Therefore it cannot be determine whether the foreign priority application, 02012515.9, has provided sufficient written description for the instant claims.

Double Patenting

6. The nonstatutory double patenting rejection stated in the previous Office Action, mail 09/22/2006, has been withdrawn in view of Applicant's amendment to the claims, filed 12/26/2006.

Claim Rejections - 35 USC § 101

Claim Rejections - 35 USC § 112, second paragraph

7. The rejections under 35 USC 101 and 112 second paragraph for claims being drawn to non-statutory subject matter, i.e., "use of ganglioside" in the previous Office Action, mail 09/22/2006, have been withdrawn in view of Applicant's amendment to the claims, filed 12/26/2006.

Claim Rejections - 35 USC § 102

8. The rejection under 35 USC 102(b) in the previous Office Action, mail 09/22/2006, has been withdrawn in view of Applicant's amendment to the claims, filed 12/26/2006.

Claim Rejections - 35 USC § 112, second paragraph

9. Claims 9-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The New Grounds of Rejection set herein is necessitated by Applicant's amendment, filed 12/26/2006.

The newly added claims are incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are the active steps required to test a biological sample for presence of anti-AG_{m1}or anti G_{m1} antibodies. Without the active steps, one of skill in the art would not be reasonably apprised of the metes and bounds of the method for prevention, inhibition and treatment of sepsis which comprises testing a biological sample for the presence of anti-AG_{m1} or anti G_{m1} antibodies.

Applicant is reminded that any amendment must point to a basis in the specification so as not o add New Matter. See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The New Grounds of Rejection set herein is necessitated by Applicant's amendment, filed 12/26/2006.

11. Claims 9-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The present claims are drawn to a method for "prevention, inhibition and treatment of sepsis in an animal or patient" comprising administering AG_{m1} as an agent. However the instant specification, as filed, does not provide sufficient enabling description for preventing or treating sepsis as encompassed by the claims because there does not appear to be sufficient in vitro or in vivo evidence to support administering Ag_{m1} to lessen or ameliorate the symptoms of sepsis.

According to *The Merck Manual of Diagnosis and Therapy*, the cause of sepsis inflammatory states resulting from systemic infection. Many factors, such as diabetes, cirrhosis, leucopenia and invasive device have been identified to predispose a person to sepsis (*The Merck Manuals Online Medical Library,* [online]. Whitehouse Station, NJ: Merck Research Laboratories, 2006-2007. [retrieved on 11/19/2007]. Retrieved from the Internet: < URL: http://www.merck.com/mmpe/print/sec06/ch068/ch068a.html>. Sepsis and Septic Shock. see pages 1-5). However, the instant disclosure does not provide sufficient in vitro or in vivo evidence showing the administration of Ag_{m1}can counter-act the cause or the manifestation of sepsis as defined by *The Merck Manual of Diagnosis and Therapy* in order to prevent or treat the disease.

One of skill in the art is well aware that sepsis is difficult to treat and the prevention, inhibition and treatment of sepsis is highly unpredictable as noted by *The Merck Manual of Diagnosis and Therapy* stating that "Trials of monoclonal antibodies to the lipid A fraction of endotoxin, antileukotrienes, and antibodies to tumor necrosis factor have been unsuccessful"(see page 5 last paragraph). Similarly, Standen et al. (*N Engl J Med* 2000, 343:447-448) also notes that sepsis or septic shock is "difficult to define, difficult to investigate, and even more difficult to treat (mortality rates are greater than 50 percent)" (see first paragraph).

Applicant appears to rely on the finding of high titers of anti- AG_{m1} and/or anti-G_{m1} antibodies in sera of septic patients for present claimed invention for preventing or treating sepsis by administering AG_{m1}. However, the specification, as filed, does not appear to provide sufficient in vitro or in vivo evidence of using AG_{m1} to counter-act symptoms or manifestation of sepsis.

The specification does not adequately teach how to effectively prevent or treat any disease or reach an appropriate beneficial therapeutic endpoint in animals or patients by administering AG_{m1}. The specification does not teach how to extrapolate data obtained from various in vitro observations to the development of effective methods of preventing or treating sepsis broadly encompassed by the claimed invention and consistent with the disclosure of various diseases and disorders disclosed on page 2 of the instant specification.

Furthermore, due to the unpredictability of sepsis, in vitro and animal model studies have not correlated well with in vivo clinical trial results in patients with sepsis. Since the therapeutic indices of immunosuppressive drugs or biopharmaceutical drugs can be species- and model-dependent, it is not clear that reliance on the in vitro and in vivo experimental observations as well as the clinical experience with targeting various inflammatory conditions with AG_{m1} accurately reflects the relative ability or efficacy of the claimed methods to prevent or treat sepsis. For example, Redl et al. (*World J Surg* 1996, 20:487-492) notes that various approaches in the development for treating sepsis, including anti-TNF antibodies and $_{anti}$-inflammatory cytokines such as IL-10 (see pages 488-489) have been proven to be valid the animal experiments, but no in clinical studies (see Conclusion).

In view of the lack of predictability of the art to which the invention pertains, the lack of established clinical protocols for effective methods to prevent and treat the scope of sepsis and inflammatory conditions, undue experimentation would be required to practice the claimed methods for prevention, inhibition and treatment of sepsis with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for preventing the diseases or disorders encompassed by the claimed methods and products.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary, the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Conclusion

12. No claim is allowed

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon Wen whose telephone number is (571) 270-3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571)272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharon Wen, Ph.D.
Patent Examiner
November 19, 2007

PHILLIP GAMBEL, PH.D JD
PRIMARY EXAMINER
TC 1600
11/20/07